BAKER BOTTS L.L.P.

Attorney Docket No.: A32011-A-PCT-USA (072448.0313)
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Antonio A. Garcia et al.			
Serial No.	:	09/807,663	Examiner	:	Tran, My Chau T.
Filed	:	July 2, 2001	Group Art Unit	:	1639
For	:	IMMOBILIZED SILVER IMMUNOASSAY SYSTEM			

DECLARATION OF ANTONIO A. GARCIA
UNDER 37 C.F.R. § 1.132

I hereby certify that this paper is being transmitted by facsimile to the United States Patent and Trademark Office, Technology Center 1600 at 703-872-9306.

8/6/04
Date of Transmission

Peter J. Shen
Attorney Name

52,217
PTO Registration No

Signature

8/6/04
Date of Signature

Commissioner for Patents
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I, ANTONIO A. GARCIA, hereby declare as follows:

1. I am a co-inventor of the invention disclosed and claimed in the present United States patent application.

2. I am an employee of Arizona State University which is the assignee of the present United States patent application.

3. Upon entry of the Reply Under 37 C.F.R. § 1.111 submitted herewith, Claims 1-9 will be pending in the present patent application.

4. Each of the pending claims requires a bioassay plate having silver ions immobilized thereon.

5. I have reviewed the Office Action mailed by the U.S. Patent and Trademark Office on May 6, 2004 for the present application. I have also reviewed U.S. Patent No. 5,552,086 to Siiman et al. ("Siiman"), U.S. Patent No. 5,232,829 to Longiaru et al. ("Longiaru"), U.S. Patent No. 4,945,057 to Temeyer ("Temeyer"), and Garcia et al., *Reactive Polymers*, 1994, 23(2-3):249-259 ("Garcia"), which were cited by the Examiner in the May 6, 2004 Office Action.

6. Siiman was cited by the Examiner as a basis for an anticipation rejection under 35 U.S.C. § 102(a). I provide this declaration in part to explain why Siiman does not disclose each and every element of the presently claimed invention. The presently claimed invention works because silver ions, attached in the manner described in the specification, retain their ability to act as "soft metal ions" and therefore can bind to the biotin molecules which are attached to the antibodies or antigens used for an immunoassay. The book by Arthur E. Martell and Robert D. Hancock "Metal Complexes in Aqueous Solution" Plenum Press 1996 reviews the scientific literature on how the ligand, by complexing the metal ion, influences the binding of that metal ion to other molecules. For example, they cite how chelation therapy is used to treat heavy metal poisoning. The most notable point being that mercury poisoning is treated with mercapto ligands which reduce the ability of mercury to bind to enzymes in the body. In an analogous sense, simply by having silver ions on the surface of silver does not make the

disclosure of Siiman relevant to the present invention. The silver ions described in Siiman are not complexed in a manner that makes them available for complexing with the sulfur atom in biotinylated antibodies. Therefore, those silver ions lack the binding properties exhibited by the silver ions of the presently claimed invention.

7. I also provide this declaration to explain why the Examiner's conclusion that the Garcia reference, in view of Temeyer, renders the present invention obvious, is unfounded. All proteins have different amounts of sulfur atoms in cysteine and methionine residues. Furthermore, proteins contain histidine residues that can also interact with silver ions, although more weakly. Accordingly, knowing how amino acids interact with immobilized silver ions cannot help the scientist anticipate how immobilized silver ions would interact with a complex protein such as an antibody. Also, biotin is attached to antibodies in the Fc region. Antibodies have two Fab regions that have antigen-binding sites which, if blocked, can block the binding of the target antigen by the antibody. Thus, one cannot *a priori* expect that antibodies with attached biotin groups would: (1) be able to bind to the biotin on the Fc region of the biotinylated antibody; and (2) maintain an active antibody for binding to the target antigen meaning that the antibody Fab regions are not interacting with the silver ions on the surface. Thus, the specific location of biotin on antibodies and their site-specific binding to antigens makes it difficult to translate the results obtained using relatively simple molecules such as amino acids to models involving complex proteins such as biotinylated antibodies.

8. In sum, I believe that Siiman does not disclose every element of the presently claimed invention. Additionally, the combination of Garcia with Temeyer does not suggest to a person of ordinary skill in the art how to successfully achieve an immunoassay

system comprising bioassay plates having silver ions directly immobilized thereon, as required by the presently claimed invention.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of any patent issuing from the above-captioned patent application.

8/5/04
Date

ANTONIO A. GARCIA